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EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,801	KLEBL ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-21, wherein the method is readable on mRNA expression in the reply filed on April 14, 2005 is acknowledged. The traversal is on the ground(s) that that the Examiner had separated Inventions I and II as being unrelated because a method for generating a genetically modified organism for drug screening comprising a step for measuring mRNA expression is materially and methodically different from the same method wherein protein expression is measured. Further, the Examiner stated that Invention I does not depend on Invention II to function and vice versa. With regards to this issue, the Examiner has considered the Applicant's arguments and has found the argument persuasive in part. The Examiner agrees that Invention II, drawn to measuring protein expression, would have to depend on presence of mRNA encoding the protein of interest. However, the issue that the Examiner was pointing out was that monitoring protein expression and mRNA expression following gene disruption or expression of a transgene comprising a gene of interest are distinct, as the art teaches while protein expression can increase, it does not necessarily depend on the fact that mRNA expression increases (e.g. see Rohlmann et al. 1998, J. Clin. Invest., 101: 689-695, below). Despite this, the Invention is drawn to the fact that there are phenotypic, cellular changes caused by the expression of a transgene of interest or caused by a disruption in a gene of interest and one way of monitoring these changes is by detecting changes in mRNA and protein levels, and thus, the

restriction between monitoring mRNA and protein (e.g. claim 10) is withdrawn. Inventions I and II of the restriction requirement are rejoined.

Applicant's election of a species in the reply filed on August 24, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant has elected "eukaryotic cell."

Claim 22 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 14, 2005.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claim 13 is objected to because of the following informalities: claim 13 has the word "lacuna" in brackets. It is unclear if "lacuna" is an amendment to another set of claims and claim 13 should have been listed as "amended". Appropriate correction is required.

Claims 4-17 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 19 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 provides for the use of a genetically modified organism, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Similarly, claim 20 does not set forth

any steps involved in the method/process and it is unclear what method process the applicant is intending to encompass.

Claims 1, 11, 12, 16, 18 are unclear. Claim 1, step b and claims 11, 12, 16, 18 use the phrase, "compensatingly differentially." The claim could be amended to read, "compensating differentially." Claims 2-17 depend on claim 1. Claims 19-21 depend on claims 17 or 18.

Claim 3 is unclear. Claim 3 uses the phrase, "one protein or protein fragment which is endogenous to the organism and/or foreign." It is unclear how an endogenous protein is foreign.

Claim 12 is unclear. Claim 12 uses the phrase, "enhanced to control." It appears that this is a typographical error and the phrase is to be read, "enhanced in control." Claim 17 depends on claim 12.

Claim 13 is unclear. Claim 13 uses the phrase, "carried out [lacuna] replacing." It is unclear what this phrase means. Claim 17 depends on claim 13.

Claim 14 is unclear. While it appears that the invention comprises reducing levels of genes which are upregulated to compensate for the changes caused by the expression of a transgene or by the disruption caused by making a knockout, it is unclear how reducing or eliminating these compensatory genes is "carried out by enhancing its expression." Claim 17 depends on claim 14.

Claim 15 recites the limitation "the reduction or elimination" in claims 1, 3, 5, 6, 7, 8, 9, 10. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 uses the phrase, "phenotype organism." It is unclear what this phrase means.

Claim 22 is missing steps a and b, as claim 22 starts with step c.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 8-10, 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Fellenberg, et al., 2001, PNAS, USA, 98: 10781-10786, as evidenced by de Almeida et al., 1999, Biol. Cell., 91: 649-663, abstract.

Fellenberg et al. teach a study identifying genes associated with the transition from mitosis to G1. In late mitosis, mitotic cyclin-dependent protein kinases have to be inactivated to exit mitosis. Cdc14p plays a major role in his transition to G1, being a dual specific phosphatase. Transgenic yeast comprising a transgene construct comprising CDC14 operably linked to an inducible promoter, GAL1, was induced to overexpressed CDC14 in the presence of galactose (Fellenberg, et al., page 10783, under "Overexpression of CDC14"). Cells were harvested for RNA preparation, labeled with radioactivity by reverse transcription, and hybridized onto a PCR-based whole genome DNA array (Fellenberg et al., page 10782, under "Sampling and Hybridization"). Fellenberg

et al. teach that genes induced upon CDC14 induction were identified. These include CDC14 itself, SIC1, and CTS1 (Fellenberg, page 10785, 1st col., 1st parag.). While not taught by Fellenberg et al., the art at the time Fellenberg et al. teaches that yeast that overexpress CDC14 exhibit cell cycle arrest, mainly in G1 (de Almeida et al., abstract). In addition to Fellenber et al. teaching the phenotype of the yeast, which is manifested as changes in gene expression as evidenced by the microarray, it is noted that the de Almeida reference was provided as evidence for claim 1, step c, for "phenotyping the organism."

Therefore, Fellenberg et al. anticipate claims 1, 3-6, 8-10, 15-17.

Claims 1, 3-6, 8, 10, 16, 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al. 2001, Am. J. Physiol. Endocrinol. Metab., 281: E857-E866.

Suzuki et al. teach the effects of aberrant expression of hormone-sensitive lipase (HSL) on cardiac lipid metabolism. Suzuki et al. teach that heart-specific HSL-overepxressing mice were generated. These transgenic mice comprise the tetracycline-controlled gene expression (Tet) wherein transgene expression is controlled by a tetracycline-responsive element (TRE), which is activated by the binding of a hybrid protein "tetracycline-responsive transcriptional activator" (tTA). tTA binds to TRE in the absence of tetracycline, resulting in the initiation of HSL transcription (Suzuki, et al., page E858, 1st col., 1st parag.). In addition to studying the physiological effects of HSL-overexpression on heart tissue, Suzuki et al. also teach the effects of HSL overexpression on cadiac gene expression

using microarray analysis. Suzuki et al. teach that a microarray analysis identified a variety of genes that were upregulated and downregulated (Suzuki et al., Table 3). Suzuki et al. teach that 400 ug of total RNA was prepared from fed or fasted MHCα-tTA and HSL-induced HBK-HSL mice (100 ug of total RNA was obtained from each animal). Total RNA was used to prepare mRNA, double strand cDNA synthesis, and biotin-labeled cRNA synthesis. The cRNA was used in the microarray study (Suzuki et al, page E859, 2nd col. under "Microarray Expression Anaylsis). It is noted that Suzuki et al. teach that changes in gene expression following HSL-expression is a phenotype detected in mouse tissue.

Thus, claims 1, 3-6, 8, 10, 16, 17 have been anticipated by Suzuki et al.

Claims 1-8, 11-14, 17, 18 rejected under 35 U.S.C. 102(b) as being anticipated by Rohlmann et al. 1998, J. Clin. Invest., 101: 689-695, as evidenced by Ishibashi et al., 1993, J. Clin. Invet., 1993, 92: 883-893.

Rohlmann et al. teach that in the liver, low density lipoprotein (LDL) receptor-related protein (LRP) and LDL receptor cooperate in removing large cholesterol-rich lipoproteins from the circulation (Rohlmann et al., page 692, 2nd col., parag. under "LDL receptor upregulation in LRP knockout livers"). Rohlmann et al. teach that there is a compensatory regulatory mechanism wherein LDL receptor expression is upregulated in LRP-deficient hepatocytes to compensate for the absence of a functional LRP-mediated removal pathway. While there was no increase in LDL receptor mRNA levels in LRP-deficient livers compared with wild-type controls, the amount of LDL receptor protein expressed

was consistently higher when LRP was absent as compared with wild-type control livers (Rohlmann et al., page 692, 2nd col., parag. under "LDL receptor upregulation in LRP knockout livers").

Rohlmann et al. teach the phenotype of mouse livers comprising a disruption in LDLR and LRP. Rohlman et al. teach that the LRP gene disruption was designed to be an inducible flox/flox construct because a homozygous disruption of LRP resulted in embryonic lethality. Rohlmann et al. teach that two animals of each of the four genotypes (LDLR-/-; LDLR-/- and LRPflox/flox; LRPflox/flox; and wild type) were injected intravenously with adenovirus comprising cre and were sacrificed 21 days later (Rohlmann et al., page 690, 2nd col., 2nd parag.). Rohlmann et al. teach that the LDLR-/- mouse was described by Ishibashi et. al. (Rholmann et al., page 689, 2nd col., 1st parag.) Ishibashi et al teach that the gene replacement vector used to generate the LDLR-/- mice was comprised of a neo resistance gene (Ishibashi, et al., page 884, 2nd col., under "Construction of gene replacement vector"). In addition to checking for LDL receptor and LRP expression following gene transfer of Cre recombinase (Rohlmann et al., 690, 2nd col., 2nd parag. and Fig. 1), Rohlmann et al. teach that mice comprising a homozygous disruption in LRP/LDLR exhibit defective remnant removal. In addition to a rise in apoB48 in plasma concentrations, mice comprising a homozygous disruption in LRP/LDLR exhibited levels of cholesterol and triglycerides that were significantly higher than mice comprising either single disruption or wild type mice (Rohlmann et al., pages 690-692 under "Defective remnant removal in LRP/LDLR double knockout animals," see also Table 1). It is

noted that the phenotype of the LRP knockout mouse is upregulation of LDL receptor.

Thus, Rohlmann et al. anticipate claims 1-8, 11-14, 17, 18.

Claim 1, 3, 5-9, 15, 17, 19, 20, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Tugendreich et al. 1999, Genome Research, 11: 1899-1912.

Tugendreich et al. teach that there is widespread recognition that the cell-based assays designed in model organisms such as the yeast S. cerevisiae provide greater ease of genetic manipulation and can be screened rapidly at low cost. Yeast cell-based assays have been designed in which mammalian proteins with yeast homologs, such as GPCRs, or enzymes such as Topoisomerase II, are made to function in yeast (Tugendreich et al. page 1900, 1st col., 2nd parag.). Tugendreich et al. teach a high throughput process in yeast that enables an artisan to assay many heterologous genes for which no suitable assay can be applied easily. In their method, Tugendreich et al teach that a phenotype readout induced by expression of a heterologous gene is established and genetic strategies to elaborate further on the phenotype or to broaden the response of yeast to a wider spectrum of heterologous cDNAs. The enhancement of the yeast phenotype is based on the synergistic of potentiating effect of such mutations (Tugendreich et al., page 1900, 2nd col., 1st parag.). Tugendreich et al. teach that their method entails: 1) a rapid, uniform, and parallel cloning method for the transfer of heterologous cDNAs into yeast expression vectors, 2) a quick method to convert high- or low- copy episomes into linear, integratable vectors,

3) an automated batch processing procedure for analyzing the data from highly sensitive liquid growth assays, 4) a random mutagenesis scheme for validation of the yeast phenotype and for structure/activity analysis of proteins that are characterized poorly or have no known active site, and 5) analysis of the selected mutants and small molecule inhibitors in mammalian secondary assays (Tugendreich et al., page 1900, 2nd col. 2nd parag.).

Tugendreich et al. teach that in their method, it is adventageous to express the cDNA of interest under the control of an inducible GAL1 promoter (Tugendreich et al., page 1901, under "A Special Yeast Expression Vector allows Rapdi Conversion of High-or Low-Copy Episomes into Integraion-Competent Vectors"). In addition to this, the assay was shown to be more responsive for screening when the GAL1-driven cDNA was expressed from a chromosomally integrated locus Tugendreich et al., page 1902, 1st col., 1st parag.). Tugendreich et al. teach that to ensure that the gene product of the expressed heterologous cDNA is full-length and properly localized in the cell, the cDNA is epitopte tagged with green fluorescent protein (GFP) (Tugendreich et al., page 1902, 2nd col. under "Recombination is used to Epitope Tag the cDNA to Determine Expression Level and the Size of the Protein Product"). Tugendreich et al. teach that a set of cDNAs was profiled in parallel (Tugendreich et al., Table 2). Table 2 shows the effect on growth interference resulting from cDNA overexpression. Tugendreich et al. teach that yeast that overexpressed one cDNA used in their screen, p38, resulted in yeast that exhibited growth interference. Tugendreich et al. teach that there was a difference in yeast growth between yeast that overexpressed p38

from a plasmid and yeast that overexpressed p38 from a construct that was integrated in the yeast genome. Plasmid-expressed p38 was expressed at higher levels than p38 expressed from an integrated construct. In order to overcome this lower level of expression, Tugendreich et al. teach that PTP2 and PTP3 were deleted from the yeast genome. This resulted in yeast that exhibited growth interference at levels at which testing of inhibitors possible (Tugendreich et al., page 1905, parag. under "Known Inhibitors of p38 Restore Growth to Yeast"). Growth was restored to yeast expressing p38 when the yeast was exposed to two inhibitors of p38, PD169316 and SB203580. It is noted that growth inhibition is the phenotype exhibited by the yeast that overexpress p38.

Thus, Tugendreich et al. anticipate claims 1, 3, 5-9, 15, 17, 19, 20, 21.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rohlmann et al. 1998, J. Clin. Invest., 101: 689-695 in view of Capecchi 1989, TIG, 5: 70-76.

Rohlmann et al. teach the phenotype of mouse livers comprising a disruption in LDLR and LRP. Rohlman et al. teach that the LRP gene disruption

was designed to be an inducible flox/flox construct because a homozygous disruption of LRP resulted in embryonic lethality. Rohlmann et al. teach that two animals of each of the four genotypes (LDLR-/-; LDLR-/- and LRPflox/flox; LRPflox/flox; and wild type) were injected intravenously with adenovirus comprising cre and were sacrificed 21 days later (Rohlmann et al., page 690, 2nd col., 2nd parag.). Rohlmann et al. teach that mice comprising a homozygous disruption in LRP/LDLR exhibit defective remnant removal. In addition to a rise in apoB48 in plasma concentrations, mice comprising a homozygous disruption in LRP/LDLR exhibited levels of cholesterol and triglycerides that were significantly higher than mice comprising either single disruption or wild type mice (Rohlmann et al., pages 690-692 under "Defective remnant removal in LRP/LDLR double knockout animals," see also Table 1). Rohlmann et al teach that it should be possible to elucidate the role of LRP or other essential genes in the formatin of atherosclerotic lesions (Rohlmann et al., page 694, 2nd col., 2nd parag.). While Rohlmann et al. teach that their double knockout model has higher cholesterol and triglyceride levels, they do not teach that their animal system could be used in a screen for substances that have an effect on the function of the heterologous protein or protein fragment.

Capecchi provides a review on making knockout mice. Capecchi also teaches the applications in which knockout mice can be used. Capecchi teaches that of more immediate application to human medicine, targeted disruptions in the mouse provide mouse models for human genetic diseases. Such models are useful in analyzing the pathology of diseases as well as provide a system for

exploring new therapeutic protocols, including gene therapy (Capecchi, page 76, 1st col., 2nd parag.).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use a mouse comprising disruptions in LRP/LDLR such that the animal could be used in a screen for substances that have an effect on reducing cholesterol and triglyceride levels.

One having ordinary skill in the art would have been motivated to use the animals in a screen for compounds that reduce atherosclerotic plaque formation.

There would have been a reasonable expectation of success given the teachings of Rohlmann et al. for teaching that mice comprising disruptions in LRP and LDLR exhibit higher triglycerides and cholesterol levels and Capecchi teaching that knockout animals are useful in screens for therapies.

Claims 19-21 rejected under 35 U.S.C. 103(a) as being unpatentable over Fellenberg, et al., 2001, PNAS, USA, 98: 10781-10786 in view of Tugendreich et al 2000, Genome Research, 11: 1899-1912).

Fellenberg et al. teach a study identifying genes associated with the transition from mitosis to G1. In late mitosis, mitotic cyclin-dependent protein kinases have to be inactivated to exit mitosis. Cdc14p plays a major role in his transition to G1, being a dual specific phosphatase. Transgenic yeast comprising a transgene construct comprising CDC14 operably linked to an inducible promoter, GAL1, was induced to overexpressed CDC14 in the presence of galactose (Fellenberg, et al., page 10783, under "Overexpression of CDC14").

Cells were harvested for RNA preparation, labeled with radioactivity by reverse transcription, and hybridized onto a PCR-based whole genome DNA array (Fellenberg et al., page 10782, under "Sampling and Hybridization"). Fellenberg et al. teach that genes induced upon CDC14 induction were identified. These include CDC14 itself, SIC1, and CTS1 (Fellenberg, page 10785, 1st col., 1st parag.). While Fellenberg et al. teach the identification of genes upon CDC14 induction, they do not teach that yeast comprising a CDC14 overexpression construct being used in a method for screening for agents that affect CDC14.

Tugendreich et al. teach that there is widespread recognition that the cell-based assays designed in model organisms such as the yeast S. cerevisiae provide greater ease of genetic manipulation and can be screened rapidly at low cost. Yeast cell-based assays have been designed in which mammalian proteins with yeast homologs, such as GPCRs, or enzymes such as Topoisomerase II, are made to function in yeast (Tugendreich et al. page 1900, 1st col., 2nd parag.). Tugendreich et al. teach a high throughput process in yeast that enables an artisan to assay many heterologous genes for which no suitable assay can be applied easily. In their method, Tugendreich et al teach that a phenotype readout induced by expression of a heterologous gene is established and genetic strategies to elaborate further on the phenotype or to broaden the response of yeast to a wider spectrum of heterologous cDNAs. The enhancement of the yeast phenotype is based on the synergistic of potentiating effect of such mutations (Tugendreich et al., page 1900, 2nd col., 1st parag.). Tugendreich et al. teach that their method entails: 1) a rapid, uniform, and parallel cloning method

for the transfer of heterologous cDNAs into yeast expression vectors, 2) a quick method to convert high- or low- copy episomes into linear, integratable vectors, 3) an automated batch processing procedure for analyzing the data from highly sensitive liquid growth assays, 4) a random mutagenesis scheme for validation of the yeast phenotype and for structure/activity analysis of proteins that are characterized poorly or have no known active site, and 5) analysis of the selected mutants and small molecule inhibitors in mammalian secondary assays (Tugendreich et al., page 1900, 2nd col. 2nd parag.).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use transgenic yeast comprising a transgene construct comprising CDC14 in a screen for compounds that affect function of CDC14.

One having ordinary skill in the art would have been motivated to use the transgenic yeast comprising the expression construct comprising CDC14 in a method of identifying compounds taught by Tugendreich et al.

There would have been a reasonable expectation of success given the teachings of Fellenberg et al. and de Almeida et al. for teaching that overexpression of CDC14 in transgenic yeast results in yeast that exhibit cell cycle arrest at G1 and given the teachings of Tugendreich et al. for teaching a method of obtaining compounds that alter the function of a protein encoded by a gene of interest (i.e. CDC14).

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center

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JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER